Claims

1. A method for administering a therapeutic molecule to a subject, comprising:

providing a hybrid protein comprising the therapeutic molecule and tetanus toxin fragment C, and

administering the hybrid protein by infusion of the hybrid protein into the cerebrospinal fluid.

2. The method of claim 1, wherein the therapeutic molecule is a protein or peptide.

3. The method of claim 2, wherein the protein is selected from the group consisting of GDNF, BDNF, LIF, cardiotrophin (CT-1), FGF, HGF, insulin-like growth factors 1 and 2 (IGF-1, IGF-2) and the neurotrophins.

4. The method of claim 1, wherein the therapeutic molecule is a nucleic acid molecule.

5. The method of claim 1, wherein the therapeutic molecule is a virus.

6. The method of claim 1, wherein the therapeutic molecule is an antibody or fragment thereof.

7. The method of claim 1, wherein the therapeutic molecule is a lipid.

8. The method of claim 1, wherein the therapeutic molecule is a polysaccharide.

9. The method of claim 1, wherein the therapeutic molecule is an oligonucleotide or a modified or derivatized oligonucleotide.

10. The method of claim 1, wherein the therapeutic molecule is an RNA molecule or a modified or derivatized oligoribonucleotide.

11. The method of claim 1, wherein the therapeutic molecule is a plasmid, cosmid, bacmid or vehicle for the packaging and/or expression of clonal DNA.

12. The method of claim 1, wherein the therapeutic molecule is a ribozyme.

13. The method of claim 1, wherein the mode of administration is intracerebroventricular administration.

14. The method of claim 1, wherein the mode of administration is intrathecal infusion.

15. The method of claim 13 or 14, wherein the hybrid protein is administered using a pump.

16. The method of claim 1, wherein the hybrid protein is infused for 1 or more days.

17. The method of claim 16, wherein the hybrid protein is infused for 3 or more days.

18. The method of claim 17, wherein the hybrid protein is infused for 1 or more weeks.

19. The method of claim 1, wherein the hybrid protein is administered to at least about 10% of brain volume.

20. The method of claim 1, wherein the hybrid protein is administered to at least about 30% of brain volume.

21. The method of claim 1, wherein the hybrid protein is administered to at least about 50% of brain volume.

22. A method for administering a therapeutic molecule to a subject, comprising:

providing a hybrid protein comprising the therapeutic molecule and tetanus toxin fragment C, and

administering the hybrid protein directly into the brain or spinal cord parenchyma.

23. The method of claim 22, wherein the therapeutic molecule is a protein or peptide.

24. The method of claim 22, wherein the protein is selected from the group consisting of GDNF, BDNF, LIF, cardiotrophin (CT-1), FGF, HGF, insulin-like growth factors 1 and 2 (IGF-1, IGF-2) and the neurotrophins.

25. The method of claim 22, wherein the therapeutic molecule is a nucleic acid molecule.

26. The method of claim 22, wherein the therapeutic molecule is a virus.

27. The method of claim 22, wherein the therapeutic molecule is an antibody or fragment thereof.

28. The method of claim 22, wherein the therapeutic molecule is a lipid.

29. The method of claim 22, wherein the therapeutic molecule is a polysaccharide.

30. The method of claim 22, wherein the therapeutic molecule is an oligonucleotide or a modified or derivatized oligonucleotide.

31. The method of claim 22, wherein the therapeutic molecule is an RNA molecule or a modified or derivatized oligoribonucleotide.

32. The method of claim 22, wherein the therapeutic molecule is a plasmid, cosmid, bacmid or vehicle for the packaging and/or expression of clonal DNA.

33. The method of claim 22, wherein the therapeutic molecule is a ribozyme.

34. The method of claim 22, wherein the hybrid protein is administered by injection.

35. The method of claim 22, wherein the hybrid protein is administered by infusion.

36. The method of claim 35, wherein the hybrid protein is administered using a pump.

37. The method of claim 35, wherein the hybrid protein is infused for 1 or more days.

38. The method of claim 37, wherein the hybrid protein is infused for 3 or more days.

39. The method of claim 38, wherein the hybrid protein is infused for 1 or more weeks.

40. The method of claim 22, wherein the hybrid protein is administered to at least about 10% of brain volume.

41. The method of claim 22, wherein the hybrid protein is administered to at least about 30% of brain volume.

42. The method of claim 22, wherein the hybrid protein is administered to at least about 50% of brain volume.

43. A method for administering a therapeutic molecule to a region of a subject's brain and spinal cord that is not accessible via retrograde transport or transsynaptic transport from motor neurons, comprising:

providing a hybrid protein comprising the therapeutic molecule and tetanus toxin fragment C, and

administering the hybrid protein by infusion of the hybrid protein into the cerebrospinal fluid.

44. The method of claim 43, wherein the therapeutic molecule is a protein or peptide.

45. The method of claim 43, wherein the protein is selected from the group consisting of GDNF, BDNF, LIF, cardiotrophin (CT-1), FGF, HGF, insulin-like growth factors 1 and 2 (IGF-1, IGF-2) and the neurotrophins.

46. The method of claim 43, wherein the therapeutic molecule is a nucleic acid molecule.

47. The method of claim 43, wherein the therapeutic molecule is a virus.

48. The method of claim 43, wherein the therapeutic molecule is an antibody or fragment thereof.

49. The method of claim 43, wherein the therapeutic molecule is a lipid.

50. The method of claim 43, wherein the therapeutic molecule is a polysaccharide.

51. The method of claim 43, wherein the therapeutic molecule is an oligonucleotide or a modified or derivatized oligonucleotide.

52. The method of claim 43, wherein the therapeutic molecule is an RNA molecule or a modified or derivatized oligoribonucleotide.

53. The method of claim 43, wherein the therapeutic molecule is a plasmid, cosmid, bacmid or vehicle for the packaging and/or expression of clonal DNA.

54. The method of claim 43, wherein the therapeutic molecule is a ribozyme.

55. The method of claim 43, wherein the mode of administration is intracerebroventricular administration.

56. The method of claim 43, wherein the mode of administration is intrathecal infusion.

57. The method of claim 55 or 56, wherein the hybrid protein is administered using a pump.

58. The method of claim 43, wherein the hybrid protein is infused for 1 or more days.

59. The method of claim 58, wherein the hybrid protein is infused for 3 or more days.

60. The method of claim 59, wherein the hybrid protein is infused for 1 or more weeks.

61. The method of claim 43, wherein the hybrid protein is administered to at least about 10% of brain volume.

62. The method of claim 43, wherein the hybrid protein is administered to at least about 30% of brain volume.

63. The method of claim 43, wherein the hybrid protein is administered to at least about 50% of brain volume.

64. A method for administering a therapeutic molecule to a region of a subject's brain and spinal cord that is not accessible via retrograde transport or transsynaptic transport from motor neurons, comprising:

providing a hybrid protein comprising the therapeutic molecule and tetanus toxin fragment C, and

administering the hybrid protein directly into the brain or spinal cord parenchyma.

65. The method of claim 64, wherein the therapeutic molecule is a protein or peptide.

66. The method of claim 64, wherein the protein is selected from the group consisting of GDNF, BDNF, LIF, cardiotrophin (CT-1), FGF, HGF, insulin-like growth factors 1 and 2 (IGF-1, IGF-2) and the neurotrophins.

67. The method of claim 64, wherein the therapeutic molecule is a nucleic acid molecule.

68. The method of claim 64, wherein the therapeutic molecule is a virus.

69. The method of claim 64, wherein the therapeutic molecule is an antibody or fragment thereof.

70. The method of claim 64, wherein the therapeutic molecule is a lipid.

71. The method of claim 64, wherein the therapeutic molecule is a polysaccharide.

72. The method of claim 64, wherein the therapeutic molecule is an oligonucleotide or a modified or derivatized oligonucleotide.

73. The method of claim 64, wherein the therapeutic molecule is an RNA molecule or a modified or derivatized oligoribonucleotide.

74. The method of claim 64, wherein the therapeutic molecule is a plasmid, cosmid, bacmid or vehicle for the packaging and/or expression of clonal DNA.

75. The method of claim 64, wherein the therapeutic molecule is a ribozyme.

76.. The method of claim 64, wherein the hybrid protein is administered by injection.

77. The method of claim 64, wherein the hybrid protein is administered by infusion.

78. The method of claim 77, wherein the hybrid protein is administered using a pump.

79. The method of claim 77, wherein the hybrid protein is infused for 1 or more days.

80. The method of claim 79, wherein the hybrid protein is infused for 3 or more days.

81. The method of claim 80, wherein the hybrid protein is infused for 1 or more weeks.

82. The method of claim 64, wherein the hybrid protein is administered to at least about 10% of brain volume.

83. The method of claim 64, wherein the hybrid protein is administered to at least about 30% of brain volume.

84. The method of claim 64, wherein the hybrid protein is administered to at least about 50% of brain volume.

85. A method for treating a neurological disorder, comprising:

administering to a subject in need of such treatment an effective amount of a hybrid protein comprising tetanus toxin fragment C and a therapeutic molecule by infusion of the hybrid protein into the cerebrospinal fluid.

86. The method of claim 85, wherein the therapeutic molecule is a protein or peptide.

87. The method of claim 85, wherein the protein is selected from the group consisting of GDNF, BDNF, LIF, cardiotrophin (CT-1), FGF, HGF, insulin-like growth factors 1 and 2 (IGF-1, IGF-2) and the neurotrophins.

88. The method of claim 85, wherein the therapeutic molecule is a nucleic acid molecule.

89. The method of claim 85, wherein the therapeutic molecule is a virus.

90. The method of claim 85, wherein the therapeutic molecule is an antibody or fragment thereof.

91. The method of claim 85, wherein the therapeutic molecule is a lipid.

92. The method of claim 85, wherein the therapeutic molecule is a polysaccharide.

93. The method of claim 85, wherein the therapeutic molecule is an oligonucleotide or a modified or derivatized oligonucleotide.

94. The method of claim 85, wherein the therapeutic molecule is an RNA molecule or a modified or derivatized oligoribonucleotide.

95. The method of claim 85, wherein the therapeutic molecule is a plasmid, cosmid, bacmid or vehicle for the packaging and/or expression of clonal DNA.

96. The method of claim 85, wherein the therapeutic molecule is a ribozyme.

97. The method of claim 85, wherein the mode of administration is intracerebroventricular administration.

98. The method of claim 85, wherein the mode of administration is intrathecal infusion.

99. The method of claim 97 or 98, wherein the hybrid protein is administered using a pump.

100. The method of claim 85, wherein the hybrid protein is infused for 1 or more days.

101. The method of claim 100, wherein the hybrid protein is infused for 3 or more days.

102. The method of claim 101, wherein the hybrid protein is infused for 1 or more weeks.

103. The method of claim 1, wherein the hybrid protein is administered to at least about 10% of brain volume.

104. The method of claim 85, wherein the hybrid protein is administered to at least about 30% of brain volume.

105. The method of claim 85, wherein the hybrid protein is administered to at least about 50% of brain volume.

106. The method of claim 85, wherein the subject has a neurological disorder selected from the group consisting of cerebrovascular accidents (stroke), amyotrophic lateral sclerosis, Parkinson's disease, Huntington's disease, Alzheimer's disease, multiple sclerosis, olivopontocerebellar atrophy, multiple system atrophy, progressive supranuclear palsy, diffuse Lewy body disease, corticodentatonigral degeneration, progressive familial myoclonic epilepsy, striatonigral degeneration, torsion dystonia, familial tremor, Down's Syndrome, Gilles de la Tourette syndrome, Hallervorden-Spatz disease, peripheral neuropathies, dementia pugilistica, AIDS dementia, age-elated dementia, age-associated memory impairment, amyloidosis-related neurodegenerative diseases, traumatic brain and spinal cord

injury, cerebral edema, schizophrenia, peripheral nerve damage, spinal cord injury, and Wernicke-Korsakoff's related dementia.

107. A method for treating a neurological disorder, comprising:

administering to a subject in need of such treatment an effective amount of a hybrid protein comprising tetanus toxin fragment C and a therapeutic molecule by administering the hybrid protein directly into the brain or spinal cord parenchyma.

108. The method of claim 107, wherein the therapeutic molecule is a protein or peptide.

109. The method of claim 107, wherein the protein is selected from the group consisting of GDNF, BDNF, LIF, cardiotrophin (CT-1), FGF, HGF, insulin-like growth factors 1 and 2 (IGF-1, IGF-2) and the neurotrophins.

110. The method of claim 107, wherein the therapeutic molecule is a nucleic acid molecule.

111. The method of claim 107, wherein the therapeutic molecule is a virus.

112. The method of claim 107, wherein the therapeutic molecule is an antibody or fragment thereof.

113. The method of claim 107, wherein the therapeutic molecule is a lipid.

114. The method of claim 107, wherein the therapeutic molecule is a polysaccharide.

115. The method of claim 107, wherein the therapeutic molecule is an oligonucleotide or a modified or derivatized oligonucleotide.

116. The method of claim 107, wherein the therapeutic molecule is an RNA molecule or a modified or derivatized oligoribonucleotide.

117. The method of claim 107, wherein the therapeutic molecule is a plasmid, cosmid, bacmid or vehicle for the packaging and/or expression of clonal DNA.

118. The method of claim 107, wherein the therapeutic molecule is a ribozyme.

119. The method of claim 107, wherein the hybrid protein is administered by injection.

120. The method of claim 107, wherein the hybrid protein is administered by infusion.

121. The method of claim 120, wherein the hybrid protein is administered using a pump.

122. The method of claim 120, wherein the hybrid protein is infused for 1 or more days.

123. The method of claim 122, wherein the hybrid protein is infused for 3 or more days.

124. The method of claim 123, wherein the hybrid protein is infused for 1 or more weeks.

125. The method of claim 107, wherein the hybrid protein is administered to at least about 10% of brain volume.

126. The method of claim 107, wherein the hybrid protein is administered to at least about 30% of brain volume.

127. The method of claim 107, wherein the hybrid protein is administered to at least about 50% of brain volume.

128. The method of claim 107, wherein the subject has a neurological disorder selected from the group consisting of cerebrovascular accidents (strokes), amyotrophic lateral sclerosis, Parkinson's disease, Huntington's disease, Alzheimer's disease, multiple sclerosis, olivopontocerebellar atrophy, multiple system atrophy, progressive supranuclear palsy, diffuse Lewy body disease, corticodentatonigral degeneration, progressive familial myoclonic epilepsy, striatonigral degeneration, torsion dystonia, familial tremor, Down's Syndrome, Gilles de la Tourette syndrome, Hallervorden-Spatz disease, peripheral neuropathies,

dementia pugilistica, AIDS dementia, age-related dementia, age-associated memory impairment, amyloidosis-related neurodegenerative diseases, traumatic brain and spinal cord injury, cerebral edema, schizophrenia, peripheral nerve damage, spinal cord injury, and Wernicke-Korsakoff's related dementia.

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